IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: Amy Juedes, Ph.D.
Cooke et al.	Art Unit: 1644
Application No.: 10/764,330	Confirmation No.: 5772
Filed: January 23, 2004	
For: Methods and Compositions for Modulating T Lymphocytes	**Declaration of Michael P. Cooke, Ph.D. under 37 C.F.R. § 1.132**

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

I, Michael P. Cooke, declare as follows:

1. I am Director of Immunology at the Genomics Research Institute of the Novartis Foundation, and am a co-inventor in the present application. I have been practicing in the field of Immunology for over fifteen (15) years. A copy of my *curriculum vitae* is attached as Exhibit 1-A.

2. I have reviewed this patent application and the da Silva *et al.* publication (*J. Biol. Chem.* 269:12521-12526 (1994)) cited by the United States Patent and Trademark Office. The cited document teaches that adriamycin inhibits inositol 1,4,5-triphosphate 3-kinase activity *in vitro*. However, the cited document is silent regarding IP3KB, or methods for identifying agents that inhibit T lymphocyte differentiation.

3. My colleagues and I tested adriamycin for inhibitory activity against IP3KB, following assays described generally in the cited document. When tested in Jurkat cells (Exhibit 1-B) or against purified ITPKb (Exhibit 1-C), our results show that adriamycin did not inhibit IP3KB.

4. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

Executed in San Diego, California, on 13th March 2007

Michael P. Cooke, Ph.D.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Cooke, Michael Paul	Director of Immunology (rank equivalent to Associate Professor)
eRA COMMONS USER NAME: none	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
University of California, Santa Barbara, CA	B.A.	8/1984	Biochemistry
University of Washington, Seattle, WA	Ph.D.	8/1991	Biochemistry
Stanford University, Stanford CA	Post-doc	9/91-2/94	Immunology

A. Positions and Honors

Positions and Employment

10/1984- 9/1986 Research Associate, HHMI -University of California, San Francisco, Dr Edward Goetzl Supervisor

9/1986- 9/1991 PhD Student, Department of Biochemistry, University of Washington, Seattle, Laboratory of Dr. Roger Perlmutter

9/1991- 2/1994 Post-doctoral fellow, Stanford University, Stanford CA; Department of Immunology, Laboratory of Dr. Christopher Goodnow

2/1994- 7/1999 Director of Genomics, SyStemix Inc, Palo Alto, CA (rank equivalent to assistant professor)

7/1999- current Director of Immunology, The Genomics Institute of the Novartis Research Foundation, San Diego, CA (rank equivalent to associate professor)

Other Experience and Professional Memberships

11/1999- current Chair - Animal Care and Use Committee, GNF

10/2004- current American Society of Hematology

1/2005- current International Society of Stem Cell Biology

Ad hoc reviewer for Science, Journal of Immunology, Stem Cells, Current Genomics, Bioinformatics

Honors

Recipient NIH pre-doctoral training grant

Recipient HHMI post-doctoral fellowship

B. Peer-reviewed publications (selected from 33 publications)

1. **Cooke, M.P**. and Perlmutter, R.M., *Expression of a novel form of the fyn proto-oncogene in hematopoietic cells.* New Biol, 1989. 1(1): p. 66-74.
2. **Cooke, M.P**., Abraham, K.M., Forbush, K.A., and Perlmutter, R.M., *Regulation of T cell receptor signaling by a src family protein-tyrosine kinase (p59fyn).* Cell, 1991. 65(2): p. 281-91.
3. Appleby, M.W., Gross, J.A., **Cooke, M.P**., Levin, S.D., Qian, X., and Perlmutter, R.M., *Defective T cell receptor signaling in mice lacking the thymic isoform of p59fyn.* Cell, 1992. 70(5): p. 751-63.
4. van Oers, N.S., Garvin, A.M., **Cooke, M.P**., Davis, C.B., Littman, D.R., Perlmutter, R.M., and Teh, H.S., *Differential involvement of protein tyrosine kinases p56lck and p59fyn in T cell development.* Adv Exp Med Biol, 1992. 323: p. 89-99.

B. Peer-reviewed publications (continued)

5. Hartley, S.B., **Cooke, M.P.**, Fulcher, D.A., Harris, A.W., Cory, S., Basten, A., and Goodnow, C.C., *Elimination of self-reactive B lymphocytes proceeds in two stages: arrested development and cell death.* Cell, 1993. 72(3): p. 325-35.
6. **Cooke, M.P.**, Heath, A.W., Shokat, K.M., Zeng, Y., Finkelman, F.D., Linsley, P.S., Howard, M., and Goodnow, C.C., *Immunoglobulin signal transduction guides the specificity of B cell-T cell interactions and is blocked in tolerant self-reactive B cells.* J Exp Med, 1994. 179(2): p. 425-38.
7. Ho, W.Y., **Cooke, M.P.**, Goodnow, C.C., and Davis, M.M., *Resting and anergic B cells are defective in CD28-dependent costimulation of naive CD4+ T cells.* J Exp Med, 1994. 179(5): p. 1539-49.
8. Rathmell, J.C., **Cooke, M.P.**, Ho, W.Y., Grein, J., Townsend, S.E., Davis, M.M., and Goodnow, C.C., *CD95 (Fas)-dependent elimination of self-reactive B cells upon interaction with CD4+ T cells.* Nature, 1995. 376(6536): p. 181-4.
9. Du, C., Redner, R.L., **Cooke, M.P.**, and Lavau, C., *Overexpression of wild-type retinoic acid receptor alpha (RARalpha) recapitulates retinoic acid-sensitive transformation of primary myeloid progenitors by acute promyelocytic leukemia RARalpha-fusion genes.* Blood, 1999. 94(2): p. 793-802.
10. Hogenesch, J.B., Ching, K.A., Batalov, S., Su, A.I., Walker, J.R., Zhou, Y., Kay, S.A., Schultz, P.G., and **Cooke, M.P.**, *A comparison of the Celera and Ensembl predicted gene sets reveals little overlap in novel genes.* Cell, 2001. 106(4): p. 413-5.
11. Su, A.I., **Cooke, M.P.**, Ching, K.A., Hakak, Y., Walker, J.R., Wiltshire, T., Orth, A.P., Vega, R.G., Sapinoso, L.M., Moqrich, A., Patapoutian, A., Hampton, G.M., Schultz, P.G., and Hogenesch, J.B., *Large-scale analysis of the human and mouse transcriptomes.* Proc Natl Acad Sci U S A, 2002. 99(7): p. 4465-70.
12. Aza-Blanc, P., Cooper, C.L., Wagner, K., Batalov, S., Deveraux, Q.L., and **Cooke, M.P.**, *Identification of modulators of TRAIL-induced apoptosis via RNAi-based phenotypic screening.* Mol Cell, 2003. 12(3): p. 627-37.
13. Wiltshire, T., Pletcher, M.T., Batalov, S., Barnes, S.W., Tarantino, L.M., **Cooke, M.P.**, Wu, H., Smylie, K., Santrosyan, A., Copeland, N.G., Jenkins, N.A., Kalush, F., Mural, R.J., Glynne, R.J., Kay, S.A., Adams, M.D., and Fletcher, C.F., *Genome-wide single-nucleotide polymorphism analysis defines haplotype patterns in mouse.* Proc Natl Acad Sci U S A, 2003. 100(6): p. 3380-5.
14. Wen, B.G., Pletcher, M.T., Warashina, M., Choe, S.H., Ziaee, N., Wiltshire, T., Sauer, K., and **Cooke, M.P.**, *Inositol (1,4,5) trisphosphate 3 kinase B controls positive selection of T cells and modulates Erk activity.* Proc Natl Acad Sci U S A, 2004. 101(15): p. 5604-9.
15. Bystrykh, L., Weersing, E., Dontje, B., Sutton, S., Pletcher, M.T., Wiltshire, T., Su, A.I., Vellenga, E., Wang, J., Manly, K.F., Lu, L., Chesler, E.J., Alberts, R., Jansen, R.C., Williams, R.W., **Cooke, M.P.**, and de Haan, G., *Uncovering regulatory pathways that affect hematopoietic stem cell function using 'genetical genomics'.* Nat Genet, 2005. 37(3): p. 225-32.
16. Sandberg, M.L., Sutton, S.E., Pletcher, M.T., Wiltshire, T., Tarantino, L.M., Hogenesch, J.B., and **Cooke, M.P.**, *c-Myb and p300 regulate hematopoietic stem cell proliferation and differentiation.* Dev Cell, 2005. 8(2): p. 153-66.
17. Zhong, J.F., Zhao, Y., Sutton, S., Su, A., Zhan, Y., Zhu, L., Yan, C., Gallaher, T., Johnston, P.B., Anderson, W.F., and **Cooke, M.P.**, *Gene expression profile of murine long-term reconstituting vs. short-term reconstituting hematopoietic stem cells.* Proc Natl Acad Sci U S A, 2005. 102(7): p. 2448-53.

Arimycin does not exhibit IP4 production in T cells

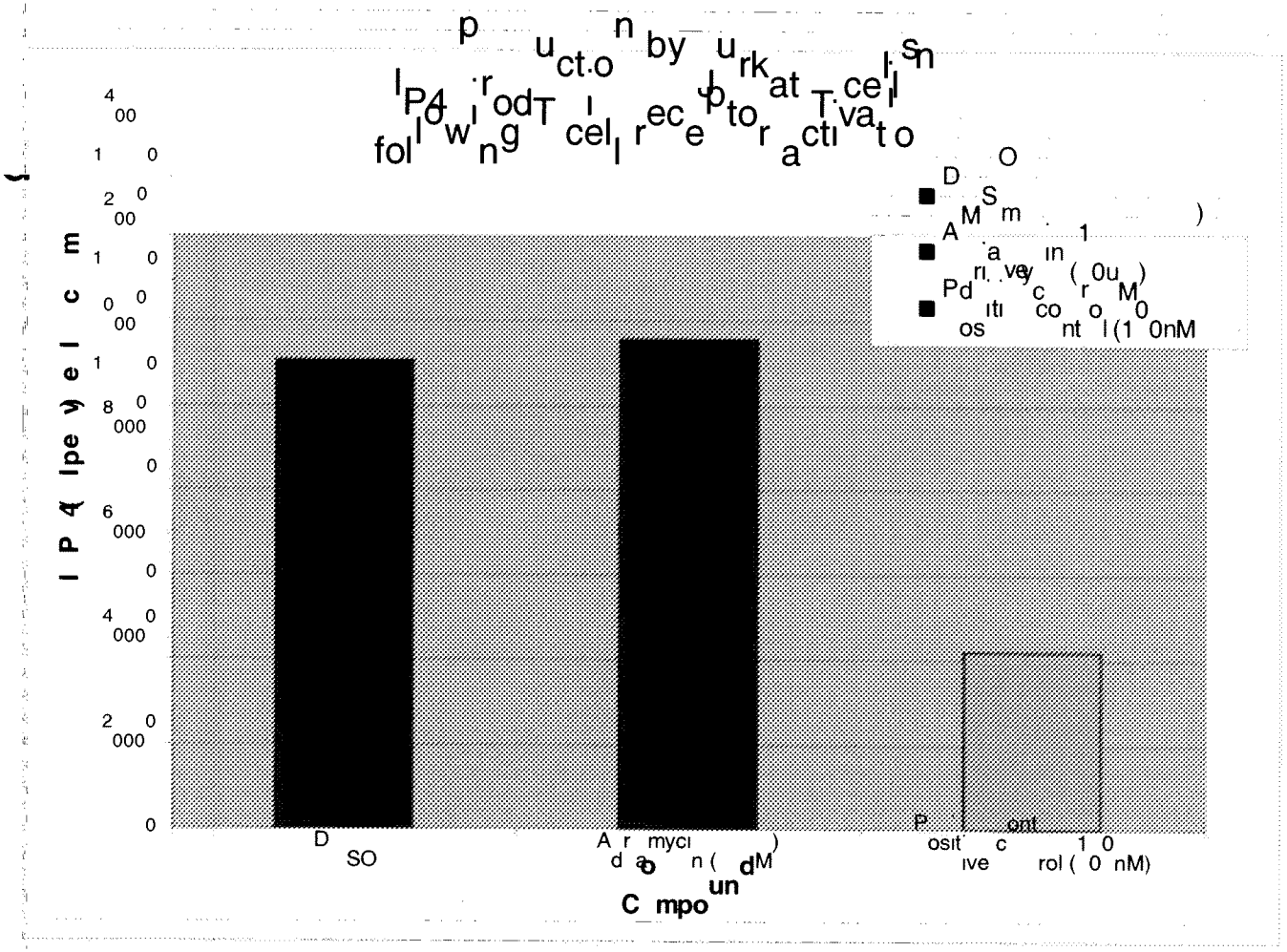

Exhibit 1-C

Adriamycin does not inhibit ITPKb enzyme activity in vitro